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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,479	10/04/2005	Pieter De Haan	285953US40 PCT	8459

22850 7590 05/14/2008

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EXAMINER	
SASAN, ARADHANA	

ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
05/14/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/528,479	DE HAAN ET AL.	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 3/5/08 are acknowledged.

2. Claims 1, 3-4 and 6-9 were amended. New claims 11-22 were added.

3. Claims 1-22 are included in the prosecution.

Response to Arguments

Objection to the Specification

4. Applicant's amendment of the Specification renders the objection moot.

Claim Objections

5. Applicant's amendments render the objections to claims 6, 8 and 9 moot.

Rejection of claims 1-10 under 35 USC § 103(a)

6. Applicant's arguments, see Page 7, filed 3/5/08, with respect to the rejection of claims 1-10 under 35 USC § 103(a) as being unpatentable over Egberink et al. (WO 02/45753) in view of Schor et al. (US 4,369,172) have been fully considered but are not found persuasive.

Applicant states that the claimed feature of "is maintained to have a water activity of at most 0.6" or the corresponding language in Claim 3 related to a water content of less than 9% w/w is critical to the claimed invention as shown in Table 2 on page 7 of the present application. Applicant states that as shown in this table, when the water activity increases above this threshold value the tablet becomes vulnerable to dust formation. Applicant argues that such a result and the threshold value is not disclosed, suggested, or even realized in either Egberink or Schor.

This is not found persuasive because although Egberink does not expressly teach the water activity of the tablet, Schor teaches a tablet with a moisture content of 4.5-5.5%. This meets the limitation of a water content of less than 9% w/w. Since the limitations of at least 55% of a cellulose ether are also obviated by the 57% of HPMC taught by Schor and 70-85% HPMC taught by Egberink, the tablet composition intrinsically meets the limitation of a tablet with a water activity of at most 0.6. Since the tablet composition is obvious over Egberink and Schor.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "maintaining a water activity of at most 0.6") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that there is no evidence of record that the "tight containers" disclosed by Egberink provide sufficient protection from moisture and that even if "tight containers" do provide some protection against moisture, such protection is less than hermetic containers, for example.

This is not found persuasive because one with ordinary skill in the art would optimize the stability of the tablets during the process of routine optimization by protecting them from moisture and would use blister packs, foil packs, bottles, desiccants, and other packaging materials used in the art to prevent moisture uptake by contents. One with ordinary skill in the art would know that the "tight containers"

disclosed by Egberink are clearly used to enhance stability of the tablets as is generally performed in the art.

Applicant argues that without any realization as to the threshold water activity or water content to remain below, there is nothing in Egberink or Schor to show how the container would satisfy this requirement. Applicant argues that the present invention differs from Schor by the fact that the tablets disclosed in the present invention are maintained to have a water activity of at most 0.6 (or a water content of less than 9% w/w). Applicant states that by decreasing the relative humidity storage condition (page 2, lines 1-3) provides an advantage in a reduction of dust formation during handling tablets (page 1, lines 31-33). There is no such suggestion in Schor et al to control the water activity in this way.

This is not found persuasive because Schor discloses a tablet with a moisture content of 4.5-5.5%. The water activity of at most 0.6 would be obvious over this moisture content. The "threshold water activity" feature is not recited in the instant claims.

Applicant argues that there is no basis to conclude that the tablets disclosed in Egberink originally have a water activity of at most 0.6 or water content when the tablets are leaving the tablet compression machine.

This is not found persuasive because Egberink is combined with Schor which discloses a tablet with a moisture content of 4.5-5.5%, therefore, intrinsically this tablet will have a water activity of at most 0.6.

Applicant argues that when viewing the combined disclosures of Egberink and Schor, the skilled artisan would not be prompted to control the water activity (or the water content) by maintaining it to a reduced level in order to avoid dust formation. Applicant argues that the combined disclosures of Egberink and Schor fail to offer any suggestion that the water activity level (or water content) should be controlled to control dust formation, what water activity level (or water content) would be the practical threshold, or how the tablet may be maintained to not exceed this threshold.

This is not found persuasive because "controlling the water activity (or the water content) by maintaining it to a reduced level in order to avoid dust formation" is a feature that is not recited in the instant claims. The water activity limitation is met by the moisture content disclosed by Schor.

Applicant argues that the moisture contained in the tablet can be used to maintain the cohesion in the tablet and thus an increase of the moisture content of the tablets once they are leaving the tablet compression machine would be considered favorably by the one skilled in the art not to have dust formation.

This statement is speculative because one with ordinary skill in the art would perform various experiments with a given active ingredient and excipients and would modify the components and process parameters, including moisture exposure, during the process of routine experimentation in order to determine which formulation and which corresponding conditions lead to minimal dust formation. Depending on the results of these experiments, one with ordinary skill in the art would make a determination about the moisture content and its relationship with dust formation.

Therefore, the rejection of 12/05/07 is maintained.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-10 remain rejected and new claims 11-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Egberink et al. (WO 02/45753) in view of Schor et al. (US 4,369,172).

The claimed invention is a packaged tablet with a matrix comprising at least 55% of a cellulose ether. The tablet has a water activity of at most 0.6 and is packaged to delay moisture uptake.

Egberink teaches a pharmaceutical formulation comprising gepirone hydrochloride, a cellulosic polymer and microcrystalline cellulose (Page 1, lines 4-7). The amount of cellulosic polymer is from 70 to 85 wt% and the amount of gepirone hydrochloride is from 13 to 21 wt% (Page 1, line 35 to Page 2, line 1). HPMC is the preferred cellulosic polymer (Page 2, lines 25-27). Example 1 discloses tablet compositions with gepirone HCl dosages ranging from 40mg to 80mg and HPMC levels ranging from 70 to 75% (Page 4, lines 15-19). The compressed tablets are stored in tight containers until further use or testing (Page 5, line 29).

Egberink does not expressly teach the water activity of the tablet.

Schor teaches a carrier base material consisting of hydroxypropylmethylcellulose (HPMC) (Col. 1, lines 12-14). This carrier base has "greater stability, greater hardness, lower friability, reduced water solubility ... from hydroxypropylmethylcellulose" (Col. 2, lines 49-53). Example 1 discloses tablets with lithium carbonate and 57% of HPMC (400mg per 702mg tablet). The tablets "had a moisture content of 4.5-5.5%" (Col. 4, lines 19-51).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a tablet with HPMC (as a cellulose ether) at 70 to 85 wt%, as suggested by Egberink, combine it with the tablet containing 57% of HPMC and with a moisture content of 4.5-5.5%, as taught by Schor, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because both the references teach tablet formulations with HPMC levels greater than 55% and with a low moisture level in the tablet and the advantages of a tablet with low moisture content include greater stability, greater hardness and lower friability (Schor, Col. 2, lines 49-51).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 1, the limitation of a packaged tablet and the limitation of delaying moisture uptake would have been obvious over the tablets that are stored in

tight containers, as taught by Egberink (Page 5, line 29). One with ordinary skill in the art would optimize the stability of the tablets by protecting them from moisture and would use blister packs, foil packs, bottles, desiccants, and other packaging materials used in the art to prevent moisture uptake by contents. The limitation of at least 55% of a cellulose ether would have been obvious over the HPMC levels of 57% taught by Schor (Col. 4, lines 19-51) and HPMC levels ranging from 70 to 75% in the example taught by Egberink (Page 4, lines 15-19). The limitation of the tablet water activity would have been obvious over the low moisture content of the tablets taught by Schor (Col. 4, lines 50-51).

Regarding instant claim 2, the limitation of the water activity of the tablet of less than 0.55 would have been obvious over the tablet containing 57% of HPMC and having a moisture content of 4.5-5.5%, as taught by Schor (Col. 4, lines 19-51).

Regarding instant claim 3, the limitation of a packaged tablet and the limitation of delaying moisture uptake would have been obvious over the tablets that are stored in tight containers, as taught by Egberink (Page 5, line 29). The limitation of at least 55% of a cellulose ether would have been obvious over the HPMC levels of 57% taught by Schor (Col. 4, lines 19-51) and HPMC levels ranging from 70 to 75% in the example taught by Egberink (Page 4, lines 15-19). The limitation of the water content of the tablet less than 9% w/w would have been obvious over the low moisture content of the tablets taught by Schor (Col. 4, lines 50-51).

Regarding instant claims 4, 7, 11 and 17, the limitation of more than 65% of a cellulose ether would have been obvious over the 70 to 85 wt% of cellulosic polymer

(HPMC levels ranging from 70 to 75% in Example 1) as taught by Egberink (Page 1, line 35 to Page 2, line 1 and Page 4, lines 15-19).

Regarding instant claims 5 and 10, the limitation of hydroxypropyl methylcellulose as the cellulose ether would have been obvious over the HPMC taught by Egberink (Page 2, lines 25-27) and Schor (Col. 1, lines 12-14).

Regarding instant claims 6, 8, 12 and 18, the limitation of 20-85mg of gepirone HCl would have been obvious over the gepirone HCl dosages (ranging from 40mg to 80mg) taught by Egberink (Page 4, lines 15-19). Egberink also teaches that the treatment regime starts with about 20mg of gepirone HCl per day and is gradually built up to 60-100mg of gepirone HCl per day (Page 2, lines 7-11). One skilled in the art would modify the quantity of the active ingredient gepirone HCl based on the desired dosage during the process of routine experimentation.

Regarding instant claim 9, the limitation of the tablet comprising 20-85mg of gepirone HCl would have been obvious over the gepirone HCl dosages (starting from 20mg and building up to 100mg) taught by Egberink (Page 4, lines 15-19 and Page 2, lines 7-11). The limitation of the tablet matrix consisting of more than 65% of a cellulose ether would have been obvious over the 70 to 85 wt% of cellulosic polymer (HPMC levels ranging from 70 to 75% in Example 1) as taught by Egberink (Page 1, line 35 to Page 2, line 1 and Page 4, lines 15-19).

Regarding instant claims 13 and 19, the limitation of microcrystalline cellulose would have been obvious over the microcrystalline cellulose taught by Egberink (Page 1, lines 4-7).

Regarding instant claims 14 and 20, the limitation of euroxide would have been obvious over the euroxide yellow or red taught by Egberink (Page 4, table with Composition of tablets).

Regarding instant claims 15 and 21, the limitation of colloidal anhydrous silicon dioxide would have been obvious over the colloidal silicon dioxide taught by Egberink (Page 4, table with Composition of tablets).

Regarding instant claims 16 and 22, the limitation of magnesium stearate would have been obvious over the magnesium stearate taught by Egberink (Page 4, table with Composition of tablets).

Conclusion

9. No claims are allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

/MP WOODWARD/
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